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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/076,618	05/12/98	PAPAHADJOPOULOS	D 02307E-07142

020350 HM12/1013
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EXAMINER	
KETTER, J	
ART UNIT	**PAPER NUMBER**
1636	6

DATE MAILED: 10/13/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Response Due 1-13-00 NS

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PTO-90C (Rev. 2/95)
*U.S. GPO: 1997-417-381/62715

2 - Mail Copy

Office Action Summary

Application No.	Applicant(s)
09/076,618	Papahadjopoulos et al.
Examiner	**Group Art Unit**
J. KETTER	1636

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 7/26/99.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-80 is/are pending in the application.

Of the above claim(s) 1-58 is/are withdrawn from consideration.

☒ Claim(s) 59-75 is/are allowed.

☒ Claim(s) 76-80 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

Applicant's election of Group IV, claims 59-80 in Paper No. 5, filed 26 July 1999, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

In particular, Applicants argue that Groups I, II and III should be rejoined to each other. However, no argument has been made regarding the elected group, Group IV. Arguments to rejoin non-elected Groups are regarded as moot, in view of their collective non-election.

Claims 1-58 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to non-elected inventions. Election was made **without** traverse in Paper No. 5.

Claims 59-75 are allowable over the prior art of record. Hansen et al. teaches, e.g., at page 137, Figure 1, Panels D and E, liposome complexes inserted with the hydrophobic domain of a linker, i.e., DSPE, which linker is attached to the hydrophilic domain of said linker, i.e., PEG, which linker is attached to a protein, i.e., an antibody, through a linkage comprising the residue of a reactive group, i.e., maleimide or hydrazide. However, Hansen et al. (U) does not teach assembly of the complex in the recited order, i.e., linkage of the protein to the linker or hydrophobic moiety, followed by mixture with the liposome to allow insertion of the hydrophobic domain/moiety into the lipid bilayer of the liposome.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

Claims 76, 77, 79 and 80 are rejected under 35 U.S.C. 102(b) as being anticipated by Hansen et al. (U).

The instant claims are drawn to a lipidic microparticle, liposome, lipid:drug complex or microemulsion droplet made by the recited method. The actual structural limitations thus claimed are: a lipidic microparticle/liposome/lipid:drug complex/microemulsion droplet inserted with the hydrophobic domain of a linker, which linker is attached to the hydrophilic domain of said linker, which linker is attached to a protein through a linkage comprising the residue of a reactive group. Lipidic microparticles, lipid:drug complexes and microemulsion droplets are all inclusive of liposomes.

Hansen et al. teaches, e.g., at page 137, Figure 1, Panels D and E, liposome complexes inserted with the hydrophobic domain of a linker, i.e., DSPE, which linker is attached to the hydrophilic domain of said linker, i.e., PEG, which linker is attached to a protein, i.e., an antibody, through a linkage comprising the residue of a reactive group, i.e., maleimide or hydrazide. It is apparent that the liposome complexes of Hansen et al. could have been assembled by the methods recited in the instant claims, i.e., attachment of the protein to the linker, followed by mixture of the protein-linker with liposomes to permit insertion of the hydrophobic domains into the lipid bilayer. The instant claims are products-by-process, and as such, are examined as the product

itself. With respect to claim 79, Hansen et al. teaches that the liposomes were, in some instances, loaded with doxorubicin.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 78 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen et al. as applied to claims 76, 77, 79 and 80 above, and further in view of Applicants' admission.

The instant claims are drawn to a lipid:nucleic acid complex made by the recited method. The actual structural limitations thus claimed are: a lipid:nucleic acid complex inserted with the hydrophobic domain of a linker, which linker is attached to the hydrophilic domain of said linker, which linker is attached to a protein through a linkage comprising the residue of a reactive group.

Hansen et al. teaches, e.g., at page 137, Figure 1, Panels D and E, liposome complexes inserted with the hydrophobic domain of a linker, i.e., DSPE, which linker is attached to the hydrophilic domain of said linker, i.e., PEG, which linker is attached to a protein, i.e., an antibody, through a linkage comprising the residue of a reactive group, i.e., maleimide or hydrazide. It is apparent that the liposome complexes of Hansen et al., in general, could have been assembled by the methods recited in the instant claims, i.e., attachment of the protein to the linker, followed by

mixture of the protein-linker with liposomes to permit insertion of the hydrophobic domains into the lipid bilayer. The instant claims are products-by-process, and as such, are examined as the product itself. Hansen et al. differs from the instant claim in not teaching specifically that nucleic acid may be loaded into the liposome.

Applicants admit, e.g., at page 2, second full paragraph, and the paragraph bridging pages 2 and 3, that it was well-known in the art to employ liposomes for the delivery of nucleic acids to cells.

It would have been obvious to one of ordinary skill in the art to have modified the liposomes of Hansen et al. to contain and thus be useful for delivery of nucleic acid to cells. The motivation to have done so would have come from the art, as shown by Applicants' admission, in that there was "enthusiasm" for use of liposomes in gene therapy.

Certain papers related to this application may be submitted to Art Unit 1805 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993)(see 37 CFR § 1.6(d)). The Art Unit 1636 Fax number is (703) 305-7939. NOTE: If Applicant *does* submit a paper by fax to this number, the examiner must be notified promptly, to ensure matching of the faxed paper to the application file, and the original signed copy should be retained by Applicant or Applicant's representative. (703) 308-4242 or (703) 305-3014 may be used without notification

of the examiner, with such faxed papers being handled in the manner of mailed responses. Applicants are encouraged to use the latter two fax numbers unless immediate action by the examiner is required, e.g., during discussions of claim language for allowable subject matter. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James Ketter whose telephone number is (703) 308-1169. The Examiner can normally be reached on Monday-Thursday from 8:00 AM-5:30 PM, and on alternate Fridays.

If attempts to reach the Examiner are unsuccessful, the Examiner's supervisor, George Elliott, can be contacted at (703) 308-4003.

James Ketter

October 9, 1999

JAMES KETTER
PRIMARY EXAMINER